UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,251	04/09/2001	Laura C. Simmons	A-63487-3/RFT/JJD	1050

7590 07/16/2003

Janet E. Hasak
Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080-4990

EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	24

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/829,251	SIMMONS ET AL.	
	Examiner	Art Unit	
	William Sandals	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,8-14 and 16-26* is/are pending in the application.

4a) Of the above claim(s) *10,12-14,16-23 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *5,6,8,9,11,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7, 16, 18, 12
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Claims 10, 12, 13-23 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 23, filed June 25, 2003.

Applicant's election with traverse of Group I, claims 5-12, 24 and 25 in Paper No. 23 is acknowledged. The traversal is on the ground(s) that Application No. 08/398,615, now US 5,840,523 contains closely related subject matter, and that the nucleic acids in instant Groups II and III have already been examined together in Application No. 08/398,615, demonstrating that there is no additional burden to search these groups which were searched together in Application No. 08/398,615. This is not found persuasive because the claims of Groups I-III have been shown to be classified in different classes and subclasses. This is demonstration of the requirement for a separate search for each Group. Further, as stated in the restriction requirement, the nucleic acids of Groups II and III are related to the instant elected Group I as a product and process of use, where the product may be used in a materially different process. These distinctions between the groups demonstrate a clear burden for examination and search. The argument is therefore not found convincing.

Applicant's have elected the species of signal sequence LamB. LamB is present in claims 8, 9, 11 and 24. Each of these claims will be examined with regard to the

elected species. Claims 10 and 12 are drawn to non-elected species, and will not be examined.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

The drawings submitted on April 9, 2001 have been approved.

Specification

The disclosure is objected to because of the following informalities: In the Brief Description of the Drawings at page 4, Figure 14 should be described as Figures 14 A and B.

Appropriate correction is required.

The amendment filed on November 30, 2001 in Paper No. 9 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Three new paragraphs are requested to be inserted at page 20, line 11. These three new paragraphs introduce new matter, describing experimental procedures which were not described previously in the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 5 and 24 are objected to because of the following informalities: At line 3, it states "initiation region variant operably linked to nucleic acid". Proper grammar dictates that the word "a" be inserted before "nucleic acid". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 6, and 24 (and dependent claims 8, 9, 11 and 25) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: The preamble recites a method of secreting a heterologous polypeptide at lines 1-2. The method steps conclude with expressing a heterologous polypeptide at line 4. The method steps therefore, do not result in the secretion of a heterologous polypeptide. Thus there is an internal inconsistency in the method. There is an omission of a secretion step in the method.

Claim 5 recites the limitation "the wild-type" in line 8. There is insufficient antecedent basis for this limitation in the claim.

Claim 6 has an internal inconsistency. At lines 2-3, it states "when said nucleic acid is operably linked to said variant". Claim 6 depends from claim 5. Claim 5 at lines 2-3 states "a transcriptional initiation region variant operably linked to [a] nucleic acid". Claim 5 does not allow for a conditional "linkage". Therefore, the stated "when said nucleic acid is operably linked to said variant" implies a conditional linkage, producing an internal inconsistency in claim 6 and one of ordinary skill in the art would not know the metes and bounds of claim 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 8, 9, 11, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Klein et al.

Klein et al. teach at the abstract, the introduction and page 515, column 2 – page 6, a secretion signal polypeptide fused to a heterologous polypeptide (bST). The secretion signal polypeptide is modified (a variant) of the wild-type secretion signal polypeptide. The fused polypeptide is expressed and secreted. The secretion signal polypeptide is LamB.

Claims 5, 8, 9, 11, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Benson et al.

Benson et al. teach at the abstract and the introduction, a secretion signal polypeptide fused to a heterologous polypeptide (LamB-LacZ). The secretion signal polypeptide is modified (a variant) of the wild-type secretion signal polypeptide. The fused polypeptide is expressed and secreted. The secretion signal polypeptide is LamB.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 6, 8, 9, 11, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein et al. in view of Goldstein et al.

The claims are drawn to a method of secreting a heterologous polypeptide of interest, in a cell, comprising using a translational initiation region variant operably linked to a nucleic acid encoding the heterologous polypeptide. The heterologous polypeptide is expressed [and secreted]. The translational strength of the variant translational initiation region is less than the translational strength of the wild type translational initiation region. The amount of secreted polypeptide produced by the variant translational initiation region is greater than the amount of polypeptide secreted

by the wild type translational initiation region. The translational initiation region contains LamB secretion signal sequence.

Klein et al. teach at the abstract, the introduction and page 515, column 2 – page 6, a secretion signal polypeptide fused to a heterologous polypeptide (bST). The secretion signal polypeptide is modified (a variant) of the wild-type secretion signal polypeptide. The fused polypeptide is expressed and secreted. The secretion signal polypeptide is LamB.

Klein et al. do not teach that the amount of secreted polypeptide produced by the variant translational initiation region is greater than the amount of polypeptide secreted by the wild type translational initiation region. Klein et al. teach the use of LamB and Omp-A secretion signal polypeptides in side by side comparisons, demonstrating the obviousness of using LamB or Omp-A to direct secretion of a heterologous polypeptide.

Goldstein et al. teach at the abstract a variant secretion signal polypeptide which induces greater amounts of secreted heterologous polypeptide than the wild type secretion signal sequence. The secretion signal sequence is Omp-A. Goldstein et al. teach at page 1230 that LamB secretion signal sequence has a comparable mechanism of action to the Omp-A secretion signal sequence, and describes the similarities of structure to argue a rationale for the increased production of the heterologous polypeptide using the Omp-A secretion signal sequence.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to substitute the Omp-A secretion signal polypeptide for the LamB secretion signal polypeptide to induce secretion of a heterologous polypeptide

because Klein et al. teach the side by side comparison of LamB and Omp-A secretion signal polypeptides for induction of secretion of a heterologous polypeptide. One of ordinary skill in the art would have been motivated to substitute the Omp-A secretion signal polypeptide of Goldstein et al. for the LamB secretion signal polypeptide of Klein et al. for the expected benefit of increasing the production of the secreted heterologous polypeptide. Further, one of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of Klein et al. who demonstrate the secretion of a heterologous polypeptide fused to a variant secretion signal polypeptide and Goldstein et al. who demonstrate the use of a secretion signal sequence to increase production of the heterologous secreted polypeptide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William Sandals whose telephone number is (703) 305-1982. The examiner can normally be reached on 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

William Sandals
July 12, 2003

JAMES KETTER
PRIMARY EXAMINER